

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : David W. Wynn et al. Confirmation No.: 7575
Appln. No. : 10/697,546
Filed : October 30, 2003
Title : CONTROLLED RELEASE ANALGESIC SUSPENSIONS
Art Unit : 1618
Examiner : Paul Micah Young

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APPEAL BRIEF

I. Real Party in Interest

The present application is assigned by virtue of an assignment recorded at reel/frame 015028/0617, to McNeil-PPC, Inc., a wholly owned subsidiary of Johnson & Johnson, a New Jersey corporation.

II. Related Appeals and Interferences

None

III. Status of the Claims

Claims 1-31 were originally presented in the application. In an amendment filed on August 9, 2007 in response to an office action dated April 9, 2007, Claims 1, 8-9, 19-22, and 26 were amended, and claims 5-7 and 10 were cancelled without prejudice. Later, in an amendment filed on October 30, 2007 in response to an office action dated October 11, 2007, Claims 1, 13-18, 26, and 31 were amended, and claims 8, 9, 11, and 12 were cancelled without prejudice. Later, in an amendment filed on May 20, 2008 in response to an office action dated January 25, 2008, claims 13, 14, 16, 18-22, 25, 26, 29, and 34 were amended, claims 1-4, 17, 23, 24, 28, 32, 33, and 35 were cancelled without prejudice, and new claims 36-46 were added. Later, in an amendment filed on October 24, 2008 in response to an office action dated August 25, 2008, Claims 26 was further amended. Lastly, in an amendment filed on May 15, 2009 in response to an office action dated February 20, 2009, Claims 26, 27, and 31 were amended, claims 25, 34, and 43-46 were cancelled without prejudice, and new claims 47-52 were added.

Claims 13-16, 18-22, 26-27, 29-31, 36-42, and 47-52 remain currently pending.

IV. Status of Amendments

A response to the final office action dated September 10, 2009 (hereinafter "Final Office Action") was filed on November 10, 2009, in which the claims were not amended. An advisory action dated December 28, 2009 (hereinafter "Advisory Action") was issued in response, maintaining the rejections.

V. Summary of the Claimed Subject Matter

Claim 26, one of the two independent claims of the above-referenced patent application, is directed to a liquid suspension dosage form comprised of (a) a first portion of particles containing an NSAID being released from the dosage form in a substantially immediate manner upon contact of the dosage form with a dissolution medium, (b) a second portion of particles containing the NSAID being released from the particles in a controlled manner upon contact of the dosage form with the dissolution medium, and (c) water, or mixtures of water

and a pharmaceutically acceptable water-miscible co-solvent selected from the group consisting of glycols, alcohols, and glycerol. The claim further states that the particles in said second portion are comprised of a core that is substantially covered by a coating thereon comprised of a controlled release composition comprising one or more enteric polymers and one or more insoluble film forming polymers wherein the weight ratio of the insoluble film forming polymer(s) and the enteric polymer(s) is from about 80:20 to about 99:1. The claim further states that the first portion of particles and said second portion of particles are suspended in component (c), wherein the pKa of said NSAID is greater than the pH of the liquid suspension pharmaceutical dosage form, and wherein the dosage form has a duration of therapeutic effect for at least about 12 hours after administration. The above claim elements are described throughout the specification, for example: the first portion of particles containing the NSAID that is released in a substantially immediate manner (“component (a)”) is described on page 6, lines 16 to 37, page 19, line 5; the second portion of particles containing the NSAID that is released in a controlled manner is described on page 7, lines 1 to 13 (“component (b)”); “the component (c)” is described on page 12, lines 1 to 3; the coated particles on component (b) coated with one or more enteric polymers and one or more insoluble film forming polymers are described one page 7, lines 27 to 36; the suspension of the particles in component (c) is described on page 15, lines 11-15; the pKa of said NSAID is greater than the pH of the liquid suspension pharmaceutical dosage form is described on page 11, lines 35-37; and the dosage form has a duration of therapeutic effect for at least about 12 hours after administration is described on page 4, lines 3-4.

Claims 13, 16, and 36, which depend from claims 26, 14, and 27, respectively, further state that the insoluble film forming polymer is selected from the group consisting of cellulose acetate, ethylcellulose, poly(ethyl acrylate, methyl methacrylate, trimethylammonioethyl methacrylate chloride) in a 1:2:0.1 weight ratio, and mixtures thereof. Such claim element is disclosed on page 8, lines 1-5.

Claims 14, 37, and 39 which depend from claims 26, 27, and 36 respectively, further state that the enteric polymer is selected from the group consisting of hydroxypropyl methylcellulose phthalate, hydroxypropyl methylcellulose acetate succinate, cellulose acetate phthalate, polyvinylacetate phthalate, polymethacrylate-based polymers, and copolymers and mixtures thereof. Such claim element is disclosed on page 8, lines 6-9.

Claims 15, 18, 38, and 40, which depend from claims 14, 16, 27, and 36, respectively, further state that the enteric polymer is selected from a poly(methacrylic acid, methyl methacrylate) in a weight ratio of 1:2 and/or poly(methacrylic acid, methyl methacrylate) in a weight ratio of 1:1. Such claim element is disclosed on page 8, lines 9-13.

Claims 19, 20, 41, and 42, which depend from claims 26, 18, 27, and 40 respectively, further state that the coated particles in said second portion are comprised of, based upon the total dry weight of the coated particles in the second portion, from about 10 percent to about 40 percent of the controlled release composition. Such claim element is disclosed on page 8, lines 21-24.

Claims 21, 22, which depend from claims 26 and 18 respectively, further state that the NSAID is a propionic acid derivative NSAID. Such claim element is disclosed on page 9, lines 36-37.

Claim 27, which depends from claim 26, further state that the dosage form comprises, based upon the total weight of the liquid suspension dosage form, (a) from about 0.25 percent to about 30 percent of a first portion containing an NSAID, (b) from about 0.0125 percent to about 0.025 percent of a second portion of particles containing said NSAID; and (c) from about 20 percent to about 70 percent of water, or mixtures of water and a pharmaceutically acceptable water-miscible co-solvent selected from the group consisting of glycols, alcohols, and glycerol. Such claim elements are disclosed on page 22, lines 17-31.

Claims 29 and 30, which depend from claims 27 and 26 respectively, state a method for treating pain in a mammal in need thereof, which comprises administering the dosage form in an amount effective for providing pain relief to the mammal for a period of at least about 12 hours after administration of the dosage form. Such claim element is disclosed on page 11, lines 7-10 and page 23, lines 1-3.

Claim 31, the other independent claims of the above-referenced patent application, is directed to a method of administering an NSAID in a pharmaceutical liquid suspension dosage form to a mammal in need thereof by providing to a mammal said dosage form such that the mammal receives an immediate release dose of said NSAID at the beginning of said 12 hour time period, and a controlled release dose of said NSAID over a period of about 12 hours after administration of said dosage form, wherein no further NSAID is provided during said 12 hour time period, wherein said dosage form comprises particles comprised of a core

that is substantially covered by a coating thereon, and said coating is comprised of a controlled release composition comprising an enteric polymer and an insoluble film forming polymer wherein the weight ratio of the insoluble film forming polymer and the enteric polymer is from about 80:20 to about 99:1 and wherein the pKa of said NSAID is greater than the pH of the liquid suspension pharmaceutical dosage form. Such method is disclosed on page 4, lines 5-12.

Claims 47-52, which depend from claims 18, 26, 29, 30, 31, and 40, respectively, further state that said NSAID is ibuprofen. Such claim element is disclosed on page 9, line 30.

VI. Grounds of Rejection to Be Reviewed.

Claims 13-16, 18-22, 25-27, 29-31, 34, and 36-46 remain rejected under 35 USC 103(a) as being unpatentable over the combined disclosures of Shah et al US Patent No. 6,126,969 (the '969 Patent) in view of Sakamoto et al US Patent No. 4,828,840 (the '840 Patent).

VII. Argument

Claims 13-16, 18-22, 25-27, 29-31, 34, and 36-46 remain rejected under 35 USC 103(a) as being unpatentable over the combined disclosures of Shah et al US Patent No. 6,126,969 (the '969 Patent) in view of Sakamoto et al US Patent No. 4,828,840 (the '840 Patent). See Pages 2-5 of the Final Office Action. Applicants respectfully disagree.

In response to the previous arguments but forth by the Applicants, the Final Office Action states that "the '969 does prefer water insoluble polymers over enteric polymers, however this preference is over enteric polymers alone. Col. 4, lin. 59 – col. 5, lin. 22 discloses several enteric polymers, as well as water insoluble polymers, Eudragit methacrylate copolymers are used in the examples, these can include either enteric polymers or not. The '969 patent suggests the use of water insoluble, pH independent polymers, but does not foreclose the inclusion of enteric polymers completely." See page 6 of the Final Office Action. Applicants again respectfully disagree and sequentially address below each of these points.

(1) First the Final Office Action states that "this preference is over enteric polymers alone." This argument assumes that the reference suggests using enteric polymers in

combination with other non-enteric polymers. This is not the case. The '969 patent clearly states that it desires a "predictable rate which is independent of inter-and intra-subject physiological variations such as pH. . . . The resulting combined immediate-release/sustained-release formulation provides higher reproducibility of drug release rates than other sustained-release dosage forms utilizing conventional enteric sustained-release coating compositions. . . . (emphasis added)" See, e.g., col. 5, lines 45-60 of the '969 Patent. Thus, it clearly states a desire to avoid using enteric polymers at all, not just avoiding the use enteric polymers by itself (e.g., a particle with just an enteric polymer coating would be a delayed release particle, not a sustained release particle).

In response to Applicant's arguments above, the Advisory Action states that "Applicant asserts that the prior art seeks a more predictable rate of release, however this disclosure is in regard to enteric polymers alone. The disclosed combination of enteric and pH independent polymers would provide the improved precision required." While this may be the case, this finding is in fact part of the Applicant's invention, not the teaching of the '969 Patent. Rather, the '969 Patent, as discussed above, states "The resulting combined immediate-release/sustained-release formulation provides higher reproducibility of drug release rates than other sustained-release dosage forms utilizing conventional enteric sustained-release coating compositions." Thus, as discussed above, the '969 Patent does not disclose the avoidance of only enteric polymers, but the avoidance of using any enteric polymer. This point is further made, as discussed above, when the '969 Patent states that it seeks to develop a dosage form "which is independent of inter-and intra-subject physiological variations such as pH."

(2) Second, the Final Office Action states the '969 patent discloses "several enteric polymers" and "Eudragit methacrylate copolymers are used in the examples, these can include either enteric polymers or not." Applicants again respectfully disagree. As discussed above, the '969 Patent actually teaches away from the use of enteric polymers. Accordingly, one of ordinary skill in the art would certainly read the disclosure of methacrylate copolymers to mean the non-enteric versions of the polymer. In fact, the only specified example of an Eudragit® polymer is Eudragit® NE30D (col. 3, line 47), which is not an enteric polymer.

In response to Applicant's arguments above, the Advisory Action states "the combination continues to disclose a combination of enteric polymers (copolymers of methacrylate and acrylic acid) and water insoluble pH independent polymers (ethylcellulose and cellulose phthalates)." However, the Advisory Action, as with the Final Office Action, fails to indicate where the '969 Patent actually teaches the use of an enteric methacrylate polymer. As discussed above, the example of a methacrylate polymer in the '969 Patent was not an enteric polymer. This is further evidenced by the fact that the '969 Patent discloses that it seeks to develop a dosage form "which is independent of inter-and intra-subject physiological variations such as pH."

(3) Third, the Final Office Action states that "the '969 patent suggests the use of water insoluble, pH independent polymers, but does not foreclose the inclusion of enteric polymers completely." The fact that a reference does not "foreclose" on the inclusion of a claim element does not mean that it teaches or suggests the claim element. As many prior art references fail to disclose elements of inventions, the issue with respect to obviousness is what the reference actually does disclose and suggest. Otherwise, a reference could be interpreted to suggest everything that it fails to specifically exclude. In any event, as discussed above, the '969 Patent actually does disclose the desire to exclude of the use of enteric polymers.

(4) Lastly, the Final Office Action addresses the Applicants previous arguments regarding the claim element of "wherein the pKa of said NSAID is greater than the pH of the liquid suspension pharmaceutical dosage form." According to the Final Office Action, "regarding the newly added pKa limitation, as discussed above since the formulation is suspended in water (ph of 7) the ibuprofen of the particles would be more acidic having a higher pKa than the suspending liquid." See page 7 of the Final Office Action. This, however, is not what the Applicants were arguing.

The Final Office Action fails to address why one of ordinary skill in the art, in reading the '969 Patent and the '840 Patent, would have been suggested to maintain the pH of a liquid suspension below the pKa of the NSAID (e.g., maintaining the suspension below a pH of 4.4 for particles containing ibuprofen). Applicants have found that maintaining the pH of the liquid suspension pharmaceutical dosage form lower than the pKa of the active agent inhibits

the NSAID from being solubilized in the suspension, which would otherwise compromise the sustained release property of the coated particles.

Accordingly, Applicants assert that the presently claimed invention would not have been obvious to a person of ordinary skill in the art at the time of the claims invention was made in light of these references. Thus, Applicants respectfully request that this rejection under 35 USC 103(a) be withdrawn.

Respectfully submitted,

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Claims Appendix

1. (Cancelled)

2. (Cancelled)

3. (Cancelled)

4. (Cancelled)

5. (Cancelled)

6. (Cancelled)

7. (Cancelled)

8. (Cancelled)

9. (Cancelled)

10. (Cancelled)

11. (Cancelled)

12. (Cancelled)

13. (Previously Presented) The dosage form of claim 26, wherein the insoluble film forming polymer is selected from the group consisting of cellulose acetate, ethylcellulose, poly(ethyl acrylate, methyl methacrylate, trimethylammonioethyl methacrylate chloride) in a 1:2:0.1 weight ratio, and mixtures thereof.

14. (Previously Presented) The dosage form of claim 26, wherein the enteric polymer is selected from the group consisting of hydroxypropyl methylcellulose phthalate, hydroxypropyl methylcellulose acetate succinate, cellulose acetate phthalate, polyvinylacetate phthalate, polymethacrylate-based polymers, and copolymers and mixtures thereof.

15. (Previously Presented) The dosage form of claim 14, wherein the enteric polymer is selected from a poly(methacrylic acid, methyl methacrylate) in a weight ratio of 1:2 and/or poly(methacrylic acid, methyl methacrylate) in a weight ratio of 1:1.

16. (Previously Presented) The dosage form of claim 14, wherein the insoluble film forming polymer is selected from the group consisting of cellulose acetate, ethylcellulose, poly(ethyl acrylate, methyl methacrylate, trimethylammonioethyl methacrylate chloride) in a 1:2:0.1 weight ratio, and mixtures thereof.

17. (Cancelled)

18. (Previously Presented) The dosage form of claim 16, wherein the enteric polymer is selected from a poly(methacrylic acid, methyl methacrylate) in a weight ratio of 1:2 and/or poly(methacrylic acid, methyl methacrylate) in a weight ratio of 1:1.

19. (Previously Presented) The dosage form of claim 26 wherein the coated particles in said second portion are comprised of, based upon the total dry weight of the coated particles in the second portion, from about 10 percent to about 40 percent of the controlled release composition.

20. (Previously Presented) The dosage form of claim 18 wherein the coated particles in said second portion are comprised of, based upon the total dry weight of the coated particles in the second portion, from about 10 percent to about 40 percent of the controlled release composition.

21. (Previously Presented) The dosage form of claim 26, wherein the NSAID is a propionic acid derivative NSAID.

22. (Previously Presented) The dosage form of claim 18, wherein the NSAID is a propionic acid derivative NSAID.

23. (Cancelled)

24. (Cancelled)

25. (Cancelled)

26. (Previously Presented) A liquid suspension dosage form comprising:

a) a first portion of particles containing an NSAID, said NSAID being released from the dosage form in a substantially immediate manner upon contact of the dosage form with a dissolution medium;

b) a second portion of particles containing said NSAID, said NSAID being released from the particles in a controlled manner upon contact of the dosage form with the dissolution medium; and

c) water, or mixtures of water and a pharmaceutically acceptable water-miscible co-solvent selected from the group consisting of glycols, alcohols, and glycerol,

wherein said particles in said second portion are comprised of a core that is substantially covered by a coating thereon, and said coating is comprised of a controlled release composition comprising one or more enteric polymers and one or more insoluble film forming polymers wherein the weight ratio of the insoluble film forming polymer(s) and the enteric polymer(s) is from about 80:20 to about 99:1, said first portion of particles and said second portion of particles are suspended in component c), wherein the pKa of said NSAID is greater than the pH of the liquid suspension pharmaceutical dosage form, and wherein the dosage form has a duration of therapeutic effect for at least about 12 hours after administration.

27. (Previously Presented) The liquid suspension dosage form of claim 26 comprising, based upon the total weight of the liquid suspension dosage form:

a) from about 0.25 percent to about 30 percent of a first portion containing an NSAID, said NSAID being released from the dosage form in a substantially immediate manner upon contact of the dosage form with a dissolution medium;

b) from about 0.0125 percent to about 0.025 percent of a second portion of particles containing said NSAID, said NSAID being released from the dosage form in a controlled manner upon contact of the dosage form with the dissolution medium; and

c) from about 20 percent to about 70 percent of water, or mixtures of water and a pharmaceutically acceptable water-miscible co-solvent selected from the group consisting of glycols, alcohols, and glycerol,

wherein the dosage form has a duration of therapeutic effect for at least about 12 hours after administration.

28. (Cancelled)

29. (Previously Presented) A method for treating pain in a mammal in need thereof, which comprises administering the dosage form of claim 27 in an amount effective for providing pain relief to the mammal for a period of at least about 12 hours after administration of the dosage form.

30. (Original) A method for treating pain in a mammal in need thereof, which comprises administering the dosage form of claim 26 in an amount effective for providing pain relief to the mammal for a period of at least about 12 hours after administration of the dosage form.

31. (Previously Presented) A method of administering an NSAID in a pharmaceutical liquid suspension dosage form to a mammal in need thereof, said method comprises providing to a mammal said dosage form such that the mammal receives an immediate release dose of said NSAID at the beginning of said 12 hour time period, and a controlled release dose of said NSAID over a period of about 12 hours after administration of said dosage form, wherein no further NSAID is provided during said 12 hour time period, wherein said dosage form comprises particles comprised of a core that is substantially covered by a coating thereon, and said coating is comprised of a controlled release composition comprising an enteric polymer and an insoluble film forming polymer wherein the weight ratio of the insoluble film forming polymer and the enteric polymer is from about 80:20 to

about 99:1 and wherein the pKa of said NSAID is greater than the pH of the liquid suspension pharmaceutical dosage form.

32. (Cancelled)

33. (Cancelled)

34. (Cancelled)

35. (Cancelled)

36. (Previously Presented) The dosage form of claim 27, wherein the insoluble film forming polymer is selected from the group consisting of cellulose acetate, ethylcellulose, poly(ethyl acrylate, methyl methacrylate, trimethylammonioethyl methacrylate chloride) in a 1:2:0.1 weight ratio, and mixtures thereof.

37. (Previously Presented) The dosage form of claim 27, wherein the enteric polymer is selected from the group consisting of hydroxypropyl methylcellulose phthalate, hydroxypropyl methylcellulose acetate succinate, cellulose acetate phthalate, polyvinylacetate phthalate, polymethacrylate-based polymers, and copolymers and mixtures thereof.

38. (Previously Presented) The dosage form of claim 27, wherein the enteric polymer is selected from a poly(methacrylic acid, methyl methacrylate) in a weight ratio of 1:2 and/or poly(methacrylic acid, methyl methacrylate) in a weight ratio of 1:1.

39. (Previously Presented) The dosage form of claim 36, wherein the enteric polymer is selected from the group consisting of hydroxypropyl methylcellulose phthalate, hydroxypropyl methylcellulose acetate succinate, cellulose acetate phthalate, polyvinylacetate phthalate, polymethacrylate-based polymers, and copolymers and mixtures thereof.

40. (Previously Presented) The dosage form of claim 36, wherein the enteric polymer is selected from a poly(methacrylic acid, methyl methacrylate) in a weight ratio of 1:2 and/or poly(methacrylic acid, methyl methacrylate) in a weight ratio of 1:1.

41. (Previously Presented) The dosage form of claim 27 wherein the coated particles in said second portion are comprised of, based upon the total dry weight of the coated particles in the second portion, from about 10 percent to about 40 percent of the controlled release composition.

42. (Previously Presented) The dosage form of claim 40 wherein the coated particles in said second portion are comprised of, based upon the total dry weight of the coated particles in the second portion, from about 10 percent to about 40 percent of the controlled release composition.

43. (Cancelled)

44. (Cancelled)

45. (Cancelled)

46. (Cancelled)

47. (Previously Presented) The dosage form of claim 18, wherein said NSAID is ibuprofen.

48. (Previously Presented) The dosage form of claim 26, wherein said NSAID is ibuprofen.

49. (Previously Presented) The dosage form of claim 29, wherein said NSAID is ibuprofen.

50. (Previously Presented) The dosage form of claim 30, wherein said NSAID is ibuprofen.

51. (Previously Presented) The dosage form of claim 31, wherein said NSAID is ibuprofen.

52. (Previously Presented) The dosage form of claim 40, wherein said NSAID is ibuprofen.

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Evidence Appendix

None

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Related Proceedings Appendix

None